AMENDMENT

In response to the office action dated December 14, 1995, please amend the above-identified application as follows:

IN THE CLAIMS

Please amend the claims as follows.

Please cancel, without prejudice, Claims 15 and 16.

Please amend Claim 1 as follows.

1. A method for the treatment of established joint inflammation in a human or non-human patient in need thereof comprising administering to the patient an effective anti-inflammatory amount of a C5 blocker, wherein the C5 blocker does not block the functions of early complement components.

REMARKS

I. Introduction

This is in response to the Office Action mailed December 14, 1995. Submitted herewith is a petition under 37 CFR §1.136(a) requesting a three month extension in which to file this amendment, and a check for $450, the required extension fee for a small entity under 37 CFR §1.17(c). With the extension, this response is due on June 14, 1996. The Commissioner is hereby authorized to charge any additional fees that may be required by this paper, or credit any overpayment, to Deposit Account No. 01-0483.

Claims 1-16 were pending in the present application. Claims 15 and 16 are hereby being canceled without prejudice

to their prosecution in a continuing application. Claim 1 is hereby being amended in order to limit the scope of the claim to only those C5 blockers that do not block the functions of early complement components. Support for this change can be found throughout applicants' specification, for example, at page 28, lines 3-4.

Applicants have noted the requirement for a petition regarding the inclusion of photographs in the figures, and will submit such a petition once allowable subject matter has been agreed to, if not sooner.

II. The §112 Rejections

The Examiner has rejected claims 2-7 and 14 under 35 U.S.C. §112 as allegedly being indefinite in their use of phrases calling for "substantial" alterations. The meaning of such "substantial" alterations is repeatedly defined in applicants' specification as indicating an alteration of at least 25%. See, for example, page 26, lines 20-21.

Applicants' therefore respectfully submit that the meaning of the phrases in question is clear, and respectfully request that the Examiner reconsider and withdraw his rejections of claims 2-7 and 14 under 35 U.S.C. §112.

III. The §102 Rejections

The Examiner has rejected claims 1-10, 14, and 15-16 under 35 U.S.C. §102 as being anticipated by Sindelar et al. (U.S. patent No. 5,173,499). All pending claims depend from

Claim 1, which, as hereby amended, requires that C5 blockers used in the methods of the invention do not block the functions of early complement components. Applicants submit that their amended claims do not read on uses of the compositions discussed by Sindelar et al. Those compositions are all relatively non-specific, and block the functions of early complement components.

The non-specificity, and early complement component blocking properties of those compounds are shown, inter alia, in Table VI of Sindelar et al. (column 41), which indicates that all tested compounds block the functions of early complement components in that they block C3a release. Although the inhibition of C3a release by K-76 COONa is reported as "only marginal," K-76 COONa is known to also block the functions of another early complement component, factor I (see Redelman et al., appended hereto as Exhibit A, particularly the title and abstract) and therefore does not fall within the scope of applicants' amended claims.

In view of the above, applicants respectfully request that the Examiner reconsider and withdraw his rejections of pending claims 1-10 and 14 under §102.

IV. The §103 Rejections

The Examiner has rejected claims 11-13 under 35 U.S.C. §103 as being obvious over the combination of the teachings of Sindelar et al (*supra*) in view of Auda et al. (Rheumatol. Int., 1990). Applicants respectfully traverse these

rejections on the grounds that the teachings of Sindelar et al. do not make any of applicants' claims obvious, and that the combination with the Auda et al. reference does not make up for this deficiency.

The discussion in the Sindelar et al. patent of possible uses for the compounds claimed therein is plainly highly speculative in nature. Applicants respectfully submit that the presence of a "laundry list" of potential diseases that might respond to treatment with the Sindelar et al. compounds cannot properly be taken to indicate that workers of ordinary skill in the art would have had a reasonable expectation of success in the use of those compounds to treat the listed diseases. Surely, no one of skill in the art would reasonably expect that these compounds would successfully treat cancer (metastasis), heart attacks, cirrhosis of the liver, meningitis, and arthritis. Sindelar et al., however, group all of these together with many other diseases that they indicate can be treated with their compounds.

In particular, Sindelar et al. indicate in the discussion under the heading "5.5. Therapeutic Uses Of The Compounds Of The Invention" (spanning columns 22-24 -- in particular at column 23, lines 7-9) that any of the conditions listed in their Table III (spanning columns 5-6) can be treated with their claimed compounds. Table III lists the following: 1) rheumatoid arthritis, 2) acute gouty arthritis, 3) acute immunological arthritis, pulmonary disorders, 4) adult respiratory distress syndrome, 5)

pulmonary disfunction-hemodialysis, 6) chronic progressive pulmonary dis-cystic fibrosis, 7) byssinosis, 8) asbestos-induced inflammation, 9) inflammation of systemic lupus erythematosis, 10) inflammation of glomerulonephritis, 11) Purtscher's retinopathy, 12) hemorrhagic pancreatitis, 13) renal cortical necrosis, 14) primary biliary cirrhosis inflammation, 15) nephropathology, 16) cranial nerve damage in meningitis, 17) tumor cell metastasis, 18) extended tissue destruction in myocardial infarction, and 19) extended tissue destruction in burns.

Surely, workers of ordinary skill did not reasonably expect that these compounds would successfully treat all of the listed disease conditions. With regard to the treatment of joint inflammation in particular, the following discussion shows why workers of skill in the art would not have expected to achieve success in the treatment of established joint inflammation using C5 blockers.

The relative contribution of complement activity to joint inflammation was a matter of considerable controversy in the art at the time that the instant application was filed. This uncertainty is discussed in applicants' specification under the subheading "Factors Associated with Joint Inflammation" spanning pages 7-11. The part of that discussion spanning page 8, line 23 to page 10 line 21 reviews the uncertainty in the art as to the importance of the contribution of complement activation to joint inflammation. That discussion further points out that the

understanding in the art of the role of complement in sustaining the inflammation of an already inflamed joint was such that the inventors themselves did not expect a successful outcome in the treatment of established joint inflammation with C5 blockers.

In fact, one of the inventors, Dr. Yi Wang, in describing his ongoing work to the scientific advisory board of Alexion Pharmaceuticals, Inc., the assignee of the instant application, on May 2, 1994, told the board that the role of complement in arthritis was controversial and that the use of C5 blockers to treat established joint inflammation would not be effective. This prediction was based upon Dr. Wang's understanding, based upon the knowledge in the art at the time, that activated T cells could maintain joint inflammation, even in the absence of complement activity. Dr. Wang therefore indicated to the board that anti-T cell agents would be required to effectively treat established disease.

Declarations by the inventors and other scientists in support of the above are being prepared, and will be submitted shortly.

In view of the above considerations, applicants respectfully submit that the present invention is not obvious, and request that the Examiner reconsider and withdraw his rejections of pending claims 11-13 under §103.

V. Conclusion

In view of the foregoing, applicants respectfully submit that the present application is now in condition for allowance. Accordingly, reconsideration and the issuance of a notice of allowance for this application are respectfully requested.

Respectfully submitted,

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